Raltitrexed (Tomudex®)

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent and Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Sodium Chloride 0.9%</td>
<td>250ml</td>
<td>Infusion</td>
<td>Fast Running</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Raltitrexed</td>
<td>3 mg/m²</td>
<td>IV Infusion</td>
<td>100ml 0.9% Sodium Chloride over 15 mins</td>
</tr>
</tbody>
</table>

**CYCLE LENGTH AND NUMBER OF DAYS**
Every 21 days for 6 cycles or until disease progression/ unacceptable toxicity

**APPROVED INDICATIONS**
Metastatic colorectal cancer
Restricted for patients unable to tolerate standard 5-FU or capecitabine based regimens, e.g. patients with Dihydropyrimidine dehydrogenase (DPD) deficiency.

**ELIGIABILITY CRITERIA**
As above

**EXCLUSION CRITERIA**
Patients with baseline renal function less than 25ml/min (Creatinine Clearance)

**PREMEDICATION**
As above

**RECOMMENDED TAKE HOME MEDICATION**
Metoclopramide 10mg three times daily as required
*Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details*

**INVESTIGATIONS / MONITORING REQUIRED**
*Pre-treatment*
Assessment of renal function, FBC, Cardiac history
*Prior to each cycle*
FBC, U&E’s, LFT’s & tumour markers as appropriate
Where CEA is elevated this should be measured before each cycle.

**ASSESSMENT OF RESPONSE**
Metastatic: Tumour size and patient symptomatic response

**REVIEW BY CLINICIAN**
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

**NURSE / PHARMACIST LED REVIEW**
On cycles where not seen by clinician.
ADMINISTRATION NOTES

- Leucovorin (folinic acid), folic acid or vitamins containing these agents must not be used immediately prior to or during administration of raltitrexed, since they may interfere with its action. There is also a theoretical potential for interaction with NSAIDS and warfarin, but no clinical evidence of a significant interaction has been found.
- Diarrhoea is common, and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem, give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily.
- Dihydropyrimidine dehydrogenase (DPD) deficiency may result in severe and unexpected toxicity to fluorouracil – stomatitis, diarrhoea, neutropenia, neurotoxicity – secondary to reduced drug metabolism. This deficiency (either significantly reduced or entirely absent) is thought to be present in about 3-5% of the population. Raltitrexed may be used as an alternative to fluorouracil or capecitabine in these patients as DPD is not involved in its metabolism.

EXTRAVASATION  See NCA / local Policy

TOXICITIES

- Diarrhoea
- Nausea and Vomiting
- Myelosuppression
- Stomatitis
- Rash
- Asthenia and fever
- Transient rises in serum transaminases

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

- Delay 1 week if ANC < 1.5 or Platelets < 100
- 25% dose reduction if ANC 0.5 – 1.0 or PLT 25 - 50.
- 50% dose reduction if ANC < 0.5 or PLT < 25.

Non- Haematological toxicity:

<table>
<thead>
<tr>
<th></th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomatitis</td>
<td>Commence corsodyl mouth wash,</td>
<td>Mouth care + Delay treatment</td>
<td>Delay chemo until recovered.</td>
<td>Delay chemo until recovered.</td>
</tr>
<tr>
<td></td>
<td>nystatin suspension</td>
<td>until recovered</td>
<td>Restart with a 25% dose</td>
<td>Restart with a 50% dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>reduction</td>
<td>reduction</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Loperamide 4mg initially, then</td>
<td>Despite correct loperamide</td>
<td>Delay chemo until recovered.</td>
<td>Delay chemo until recovered.</td>
</tr>
<tr>
<td></td>
<td>2mg after each motion</td>
<td>treatment, delay treatment</td>
<td>Restart with a 25% dose</td>
<td>Restart with a 50% dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>until recovered</td>
<td>reduction</td>
<td>reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Discuss with SpR/Consultant)</td>
<td></td>
</tr>
</tbody>
</table>
Renal dysfunction:
For patients with abnormal serum creatinine before treatment or on any subsequent cycle of treatment, check creatinine clearance and modify dose as follows:

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Dose</th>
<th>Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 65ml/min</td>
<td>Full</td>
<td>Three weekly</td>
</tr>
<tr>
<td>55-65ml/min</td>
<td>75%</td>
<td>Four weekly</td>
</tr>
<tr>
<td>25-55ml/min</td>
<td>% equivalent to creatinine clearance, e.g., if 30 mL/min give 30% of full dose</td>
<td>Four weekly</td>
</tr>
<tr>
<td>&lt; 25ml/min</td>
<td>No therapy</td>
<td>No therapy</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION
Can be given at Cancer Centre or Cancer Unit

REFERENCES: